

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

To:
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Date of mailing
(day/month/year) **01 JUN 2009**

Applicant's or agent's file reference
39833

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/IL07/00918

International filing date (day/month/year)
19 July 2007 (19.07.2007)

Priority date (day/month/year)

International Patent Classification (IPC) or both national classification and IPC
IPC: **A61K 51/00**(2006.01);**A61N 5/00**(2006.01)
USPC: 424/1.11;604/403

Applicant
SPECTRUM DYNAMICS

1. This opinion contains indications relating to the following items:

- | | | |
|-------------------------------------|--------------|--|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the opinion |
| <input type="checkbox"/> | Box No. II | Priority |
| <input checked="" type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input checked="" type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> | Box No. VI | Certain documents cited |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US
Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
Facsimile No. (571) 273-3201

Date of completion of this opinion
01 September 2008 (01.09.2008)

Authorized officer *J. Hurley*
MARIA B. MARVICH
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Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of:

☒ the international application in the language in which it was filed

☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ on paper

☐ in electronic form

c. time of filing/furnishing

☐ contained in the international application as filed.

☐ filed together with the international application in electronic form.

☐ furnished subsequently to this Authority for the purposes of search.

4. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 290-295, 359, 362, 363, 367, 371, 372, 380-382, 384, 449-540 and 578-582

because:

☒ the said international application, or the said claim Nos. 428-448 relate to the following subject matter which does not require an international search (*specify*):

because the claimed recitation of a use without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 USC 101.

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 290-295, 359, 362, 363, 367, 371, 372, 380-382, 384, 449-540 and 578- are so unclear that no meaningful opinion could be formed (*specify*):

A multiply dependent claim cannot depend from another multiply dependent claim

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

☐ no international search report has been established for said claims Nos. _____

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13ter.1(a) or (b).

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details.

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Box No. IV Lack of unity of invention

1. ☐ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has, within the applicable time limit:
- ☐ paid additional fees
 - ☐ paid additional fees under protest and, where applicable, the protest fee
 - ☐ paid additional fees under protest but the applicable protest fee was not paid
 - ☐ not paid additional fees
2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
 - ☒ not complied with for the following reasons:
See the lack of unity section of the International Search Report (Form PCT/ISA/210)

4. Consequently, this opinion has been established in respect of the following parts of the international application:
- ☐ all parts.
 - ☒ the parts relating to claims Nos. 1-289,296-358,360,364-366,368-370,373-379,383,385-448,541-577 and 583-588

**WRITTEN OPINION OF THE
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Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>Please See Continuation Sheet</u>	YES
	Claims <u>Please See Continuation Sheet</u>	NO
Inventive step (IS)	Claims <u>Please See Continuation Sheet</u>	YES
	Claims <u>Please See Continuation Sheet</u>	NO
Industrial applicability (IA)	Claims <u>Please See Continuation Sheet</u>	YES
	Claims <u>Please See Continuation Sheet</u>	NO

2. Citations and explanations:

Claims 252 and 253 lack novelty under PCT Article 33(2) as being anticipated by Jackson et al (US 20040086437; see entire document).
Jackson et al teach methods of packaging and packaged radiopharmaceuticals such as ¹³N ammonia or ¹⁵O water (see e.g. abstract and ¶ 0004 and 0025).

Claims 254-261, 267, 385-388 and 566 lack novelty under PCT Article 33(2) as being anticipated by Liu et al (US 20070166227). Liu et al teach for example that Tc99m compounds are between 0.05-5 mCi (see e.g. ¶ 233). Liu et al also teach use of dual radiolabels that are different from each other (see e.g. ¶ 0139).

Claims 541, 552 and 583-588 lack novelty under PCT Article 33(2) as being anticipated by Belardinelli et al (US 20050020915; see entire document).

Bellardinelli et al teach compositions and methods of administration of a first and second radiopharmaceutical wherein stress is applied prior to the second and then radioimaging (see e.g. ¶ 0242).

Claims 283-286 and 289 lack an inventive step under PCT Article 33(3) as being obvious over Liu et al (20070166227) in view of Ruosso et al (20050205792).

Liu et al in view of Ruosso et al teach compositions and methods of imaging myocardial reperfusions with dual radiopharmaceuticals (see Liu et al ¶ 0139, 0233 and Ruosso et al figure 7 and ¶ 0086).

Claims 1-251, 262-266, 268-272, 275, 287, 288, 296-358, 360, 361, 364-366, 368-370, 373-379, 383, 389-427, 542-551, 553-565, 567-577 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the specific components of doses and combinations as set forth in the claims.

Claims 1-276, 283-289, 296-358, 360, 361, 364, -366, 368-370, 373-379, 383, 385-427, 541-577, 583-588 meet the criteria set out in PCT Article 33(4), and thus meet industrial applicability because the subject matter claimed can be made or used in industry.

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

V.I. Reasoned Statements:

The opinion as to Novelty was positive (Yes) with respect to claims 1-251, 262-266, 268-272, 275, 283-288, 296-358, 360, 361, 364-366, 368-370, 373-379, 383, 389-427, 542-565, 567-577

The opinion as to Novelty was negative (No) with respect to claims 252-261, 267, 273, 274, 276, 385-388, 541, 552, 566, 583, 584, 586, 587

The opinion as to Inventive Step was positive (Yes) with respect to claims 1-251, 262-266, 268-272, 275, 287, 288, 296-358, 360, 361, 364-366, 368-370, 373-379, 383, 389-427, 542-565, 567-577

The opinion as to Inventive Step was negative (NO) with respect to claims 252-261, 267, 273, 274, 276, 283-286, 289, 385-388, 541, 552, 566, 583, 584, 586, 587

The opinion as to Industrial Applicability was positive (YES) with respect to claims 1-227, 283-289, 296-358, 360, 361, 364-366, 368-370, 373-379, 383, 385-427, 541-577, 583-588

The opinion as to Industrial Applicability was negative (NO) with respect to claims NONE